REMARKS

Reconsideration of this application is respectfully requested.

As an initial matter, Applicant would like to thank the Examiner for courtesies extended to Applicant's representative during the telephone interview of September 4, 2008. Claims 1, 5, 6, and 54-55 are in the application. Through this amendment, claim 1 has been amended to incorporate the limitations of claim 3, which has been canceled herein. New claims 54 and 55 have been added, which recite that the epoxy-activated insoluble support is not cross-linked, and that the epoxy activated insoluble support is agarose, respectively. Support for these amendments may be found, for example, at paragraph [0071] of the application. In addition to claim 3, claims 2, 4 and 24-31 have been cancelled.

In the Official Action, the Examiner rejected claims 1, 2, 4, 6 and 24-27 under 35 U.S.C. §103(a) as being allegedly unpatentable over Sjoholm et al. (U.S. Patent No. 4,061,466) in view of Spring et al. (U.S. Patent No. 5,643,721) and further in view of Degen et al. (U.S. Patent No. 5,567,615). The Examiner admitted that "Sjoholm et al. fail to teach the ligand attached to the support via an epoxy linkage." The Examiner relied on Spring et al. and Degen et al. for allegedly overcoming this deficiency.

Through this Amendment, the Applicant has amended independent claim 1 to recite the limitations of original claim 3. Claim 3 was not rejected on this basis, and thus it is respectfully asserted that the rejection as to claim 1 has been overcome. The Applicant has canceled claims 24-27, thus rendering the remainder of this rejection moot. It is therefore submitted that claim 1, and those claims dependent thereon, are patentable over Sjoholm et al., Spring et al., and Degen et al., whether taken alone or in combination.

The Examiner then rejected claims 1-6 and 24-27 under 35 U.S.C. §103(a) as being allegedly unpatentable over Grahnen et al. (Eur. J. Biochem., 80, 573-580 (1997)) in view of

Spring et al. and further in view of Degen et al. The Examiner admitted that "Grahnen et al. fail to teach the ligand attached to the support via an epoxy linkage" and relied on Spring et al. and Degen et al. for allegedly overcoming this deficiency.

Applicant respectfully submits that none of Grahnen et al., Spring et al., or Degen et al. disclose an apparatus in which the ligand is used to bind to albumin, which is specifically set forth in the present claims. Grahnen et al. is directed to a method of preparation of ligandin with glutathione-*S*-transferase activity from porcine liver cytolsol. Grahnen et al. do not teach a method or apparatus for binding albumin. Neither Spring et al. nor Degen et al. disclose an apparatus to bind albumin, and thus neither reference remedies the defects of Grahnen et al.

Further, Grahnen et al. specifically discloses the use of a particular, cross-linked support to bind a ligand. As set forth at p. 574 of Grahnen et al., sepharose 4B is first cross-linked with 2,3-dibromopropanol to produce Sepharose CL-4B (the "CL" stands for cross-linked). As further evidence that the sepharose in Grahnen et al. must be cross-linked, Grahnen et al. states that "when bromosulphophthalein was treated ***without*** Sepharose CL under identical conditions at 100°C, only insignificant changes were seen in the ultraviolet and visible absorption spectra." (Page 574). (Emphasis added).

As set forth in the Sigma-Aldrich Product Information Document (Exhibit A), there is a clear distinction between non-cross-linked Sepharose (such as Sepharose 2B, Sepharose 4B and Sepharose 6B) and cross-linked Sepharose (such as Sepharose CL-2B, Sepharose CL-4B and Sepharose CL-6B). According to the Product Information Document (Exhibit A), after cross-linking, the Sepharose gel is desulfated by alkaline hydrolysis under reducing conditions, which results in cross-linked polysaccharide chains that have a very low content of ionizable groups. In fact, the Product Information Document states that cross-linked Sepharose provides higher chemical stability. Therefore, the structure and functionality of cross-linked Sepharose, such as that used in Grahnen et al., are very specific. See MPEP §2141.02(VI) ("A prior art reference

must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.").

Under the explicit requirements set forth under *KSR*, the Examiner may not alter the function of the elements upon which the Examiner relied on in an obviousness rejection. As such, Grahnen et al. cannot be modified to avoid the use of cross-linking. Cross-linking is expressly shown in Grahnen et al. as producing a better result. See MPEP §2143.01(VI) ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.").

The Examiner noted that the claims do not exclude the presence of cross-linked agarose. However, it is completely unclear how an epoxy-activated support would perform under cross-linking conditions. Under *KSR*, a finding of obviousness requires:

> A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with **no change in their respective functions**, and the combination would have **yielded nothing more than predictable results** to one of ordinary skill in the art.

(Emphasis added).

It is not clear if the function of Grahnen et al. changes by combining epoxy-activation; in particular, it is unclear if the epoxy-activation alters the functionality of the cross-linking. Moreover, there is no predictability as to what results can be achieved. It is respectfully submitted that claim 1, along with dependent claims 5, 6, 54 and 55, are patentable over Grahnen et al., Spring et al. and Degen et al., each taken alone or in combination.

It is noted that newly added claims 54 and 55 specifically recite that the epoxy-activated insoluble support is not cross-linked. A reading of the specification as filed provides ample

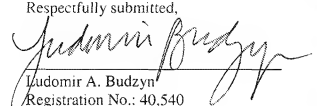
support for this limitation. In Example 1 of the application, the apparatus incorporates Sepharose 6B as the insoluble support. As explained in the aforementioned Sigma-Aldrich Product Information document (Exhibit A), Sepharose 6B and Sepharose CL-6B are considered two distinct and separate products. Sepharose 6B is a "beaded agarose gel filtration medium". In contrast, Sepharose CL "is a cross-linked derivative of Sepharose." The application as filed specifically uses Sepharose 6B, which is a non-cross-linked agarose product.

As explained above, Grahnen et al. specifically rely upon the use of Sepharose CL-4B, which is a cross-linked agarose product. It would be improper to modify Grahnen et al. to use a non-cross-linked product (such as Sepharose 6B). Thus, it is respectfully submitted that newly added claims 54 and 55 provided additional bases of patentability over Grahnen et al., Spring et al., and Degen et al.

Finally, the Examiner rejected claims 24 and 27-31 under 35 U.S.C. §103(a) as being allegedly unpatentable over Pieper et al. (U.S. Published Patent Application No. 2002/0127739) in view of Grahnen et al., and further in view of Spring et al. and further in view of Degen et al. The Examiner admitted that Pieper et al. fail to teach a ligand of bromosulfophthalein. The Examiner relied on Grahnen et al. for allegedly overcoming this deficiency. The Examiner further relied on Spring et al. and Degen et al. for the alleged notion of substituting an epoxy linkage. Through this Amendment, the Applicant has canceled claims 24 and 27-31, thus rendering this rejection moot.

Favorable action is earnestly solicited. If there are any questions or if additional information is required, the Examiner is respectfully requested to contact Applicant's attorney at the number listed below.

Respectfully submitted,



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